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Comprehension and personal value of negative non-diagnostic genetic panel testing

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Abstract

Increasing interest and pursuit of genetic testing by the general public have raised concerns about their understanding and use of their results. While most research has focused on individuals receiving positive genetic test results, there have been limited investigations assessing the understanding and utility of receiving negative genetic test results. Individuals who receive a negative (or uninformative) genetic test result may not appreciate the limitations of genetic testing and their residual disease risk. The goals of this study were to explore participant understanding and perceived utility of negative non-diagnostic genetic test results. We conducted semi-structured interviews with participants who received negative non-diagnostic genetic test results from the electronic Medical Records and Genomics Network (eMERGE) testing panel at Northwestern University. A total of 17 participants were interviewed. While many expressed a lack of understanding of genetics and the relationship between genes, disease, and environment, most acknowledged that they had residual risk to develop a health problem and should continue with their routine health management. Additionally, participants expressed that their negative results had personal value, by providing them peace of mind and learning additional knowledge about themselves and their health. Participants did not anticipate that results would have an impact

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AUTHOR CONTRIBUTIONS

MS, SA, and CH contributed to the conception, design, analysis, and interpretation of data and critical revision of the manuscript. NN contributed to design, analysis, interpretation of data, and drafting of the manuscript. MM contributed to interpretation of data and critical revision of the manuscript. All authors approve the final manuscript.

Conflict of interest

Author Christin Hoell, author Sharon Aufox, author Nora Nashawaty, author Melanie Myers, and author Maureen Smith declare they have no conflicts of interest.

Human Studies and Informed Consent

This study is approved by the Northwestern University Institutional Review Board (STU00201671). All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was obtained from all participants prior to being included in the study.

Animal Studies

No non-human animal studies were carried out by the authors for this article.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

on their lifestyle, but felt the results were useful for sharing with their physician and could inform future genetic testing decisions. While mostly positive, some participants were disappointed not to learn more individualized results. While a more thorough exploration is necessary, findings in this study can aid efforts to improve or innovate informed consent for genomic testing, as well as scalable modes of result return that foster comprehension following negative genetic testing.

Keywords

genetic testing; health behavior; negative results; perceived utility; population screening; understanding

1 | INTRODUCTION

Genetic testing has become increasingly available to the general public through direct-to-consumer (DTC) health and ancestry testing (Tandy-Connor et al., 2018) and has allowed access to genetic tests that were previously only offered to an ‘at-risk’ population. In addition, a number of large-scale research opportunities, such as the All of Us Research Program and Geisinger’s MyCode, have resulted in increasing numbers of the general population receiving genetic testing (Singer, 2018). Undoubtedly, the availability of genetic testing in the general population will identify a small percentage of individuals not previously known to be at risk for genetic conditions (Dorschner et al., 2013; Yang et al., 2014). However, the vast majority of individuals participating in genetic testing outside of a clinical setting will receive ‘negative’ or ‘uninformative’ results (referred to hereafter as negative results).

Along with the growing interest in genetic testing is the increasing complexity of genetic testing and testing options, ranging from whole genome or whole exome analysis, to panels of multiple genes, to polygenic risk scores, all of which can provide different types and amounts of genetic information. The average consumer, patient, or research participant has little to no background knowledge from which to discern the differences between these tests (Burke, Coughlin, Lee, Weed, & Khoury, 2001; Haga et al., 2013). Several investigators have raised concerns about the questionable value of non-diagnostic genetic testing, as well as the potential for harm and misunderstanding of these results. Specifically, concerns relate to the nuance of negative results, particularly the potential for over and under interpretation of a negative result, as well as the potential for future reinterpretation of variants (Brothers, Vassy, & Green, 2019; Butterfield et al., 2019; Yurgelun, Hiller, & Garber, 2015).

The incorrect interpretation of negative results may be particularly concerning when results are returned without the benefit of genetic counseling. Recommendations for diagnostic genetic testing have generally included providing pre- and post-test genetic counseling (Hershberger et al., 2018). Reasons for this approach in the clinical setting include a higher chance for results to be positive, possible recommendations for additional genetic testing for the patient or family members, as well as psychosocial and medical ramifications of receiving a positive result or a negative result in a person with a condition or a positive family history. Pre- and post-genetic counseling is not routinely performed in the context of non-diagnostic genetic testing. Therefore, many researchers and clinicians have provided

recommendations regarding ways to better communicate genetic information in a written or online report (Butterfield et al., 2019; Haga et al., 2014; Nightingale et al., 2019; Recchia, Chiappi, Chandratillake, Raymond, & Freeman, 2020). However, few studies have explored the impact on the recipient of receiving non-diagnostic negative results, including how the results are understood and their long-term effect on screening and health behaviors. As a result, uncertainty remains as to individuals' understanding of residual risk due to genetic heterogeneity and the multifactorial nature of many health conditions. Also unclear is whether individuals will continue with recommended screenings and health behaviors after receiving negative results.

Northwestern University is one of ten eMERGE (electronic **M**edical **R**ecords and **G**enomics) III Network clinical sites offering research participants the return of results from a network-wide gene panel and assessing participant comprehension, use and perceived value of genetic test results, as well as the development and implementation of best practices for the sharing of genetic information between participants and healthcare providers (Burke et al., 2001). At the Northwestern site, 3,000 patients of Northwestern Medicine were recruited to receive both positive and negative results from genomic sequencing. The purpose of this study was to qualitatively assess participants' reactions, their understanding, and their opinions about the utility of their negative genetic test results.

2 | METHODS

2.1 | Participants and recruitment

In order to be eligible for the eMERGE III study at Northwestern University, individuals had to have an electronic medical record in the Northwestern Memorial Healthcare system, be at least 18 years old, and speak and read English or Spanish. Eligibility was not based on health status, and personal and family history information was not collected. Both genetic counselors and research coordinators who were not genetic counselors conducted the informed consent process. Participants did not receive pre-test genetic counseling. A consent checklist used during the recruitment encounter included the following topics: The types of results that would be available, including a description of the broad categories of conditions (i.e., cancer and cardiovascular conditions), potential risks, benefits, and limitations of participation, and how the participant's privacy and confidentiality would be protected. Participation involved a blood draw for genetic testing, a survey to collect demographic information as well as other baseline measures not used in this study, and consent to receive genetic test results and have them placed in their electronic health record. Additionally, participants were provided the option to be surveyed and/or interviewed after they received the genetic test results.

eMERGE III participants with negative genetic test results (defined as no pathogenic or likely pathogenic variants identified) were notified by mail. The mailing included a copy of their result report, a cover letter explaining the results, a list of genetic terms and definitions, and a link to the study webpage that contained additional details about the genes and associated conditions that were included in the test. Participants with positive genetic results (defined as pathogenic or likely pathogenic variant identified) had their results returned over

the phone or in person by a study genetic counselor and received a follow-up summary letter with a copy of their results.

This study aimed to interview Northwestern eMERGE III participants who received negative results. The recruitment period lasted from January 2018 to March 2018. Participants were eligible if they had agreed to be interviewed during eMERGE III enrollment and were mailed their negative results within the previous 4-8 weeks. The racial and ethnic diversity of the interview participant pool was enriched by using results from our baseline survey to over-select black and Hispanic participants. Fifty-two eligible participants were emailed an interview invitation. If no response was received to the initial invitation, a follow-up email was sent one week later. Study participants were offered a \$50 Visa gift card as compensation for their time. The current study was approved by the Northwestern University Institutional Review Board (STU00201671).

2.2 | Genetic testing panel

Genetic testing in the eMERGE study involved sequencing 109 genes and approximately 1400 SNPs that were chosen by consensus by the eMERGE Network. From the list of genes and SNPs, the Northwestern investigators chose to return the 56 genes recommended by ACMG as being clinically actionable, as well as an additional 32 genes and 28 SNVs (ACMG Board of Directors, 2015; eMERGE, 2019; Green et al., 2013). Conditions associated with these genes and SNVs included hereditary cancer syndromes, cardiac conditions, neurologic conditions, and a variety of other disorders. Variants of uncertain significance were not returned.

2.3 | Data collection and analysis

A semi-structured interview guide was developed focusing on the following areas: previous genetic testing and genetic counseling experiences, understanding of the genetic and risk information provided in the result report and cover letter, reactions to and expectations of the testing, and utility of the results. Demographic information was obtained from the baseline survey (e.g., age, sex, race, ethnicity, level of education, income, and history of genetic testing), and during the interview (e.g., religiosity and employment in the healthcare industry).

All interviews were conducted over the phone by one investigator (NN) and were recorded and transcribed. This study used a constant comparative method to analyze the transcript data with inductive coding (Corbin & Strauss, 1990). All transcripts were manually coded and analyzed by NN. The first three transcripts were also coded by CH and MS to create the coding scheme and ensure consistency of code application and definition. After the codebook was established, CH coded every third transcript to ensure inter-coder reliability. Discrepancies were discussed until consensus was achieved (MacQueen et al., 1998). Saturation was defined by the non-emergence of new codes (Saunders et al., 2018).

3 | RESULTS

3.1 | Participants

Of the 52 individuals invited to participate in an interview, 17 consented to participate (33% response rate). Interviews lasted an average of 35 minutes (range 25 to 55 minutes). Table 1 shows participant demographics. The majority of participants were female (82%) with an average age of 53 years. Seven participants identified as white (41%), five identified as black (29%), and five identified as Hispanic (29%). All participants reported at least completing some college education or more, with most holding a college degree ($n = 7$) or a postgraduate degree ($n = 7$). Most participants (82%) had no prior experience with genetic testing.

3.2 | Themes

We report here on seven unique themes identified in our study and grouped under two domains: comprehension and personal value (Table 2).

3.3 | Participant comprehension

Two themes were identified related to participant comprehension: knowledge of genetic concepts and understanding of residual risk. Many participants lacked confidence in their understanding of the meaning of their negative test results, and some had potential misconceptions about the mechanisms of mutation and disease etiology. However, nearly all were able to demonstrate an understanding of residual risk.

3.4 | Knowledge of genetic concepts

Participants often expressed a lack of knowledge of genetics or a lack of confidence in their understanding of genetics. This often led to participants being hesitant or unsure of the meaning of their negative test result. Regardless of their educational level, participants referred to their own lack of knowledge when asked questions such as the meaning of a negative test results and possible sources of residual risk.

It looked okay, I think, for me, but I'm not knowledgeable.

(P14, 57-year-old, female)

Upon further discussion of their results, some participants attempted to introduce and explain genetic concepts even after expressing their lack of knowledge. One concept that participants often brought up was that genes could change. Participants seemed to be conflating ideas about mutation and gene expression, as well as their understanding of how a genetic alteration happens and how it leads to disease:

Uhh well I think that your genes can change. Maybe they're fine right now, but maybe ten or twenty years down the road you know they wouldn't. So I honestly don't know too much about the medical field at all so I don't know how any of that stuff works.

(P2, 49-year-old, female)

Uncertainty about the stability of genomic information led some participants to think that re-taking the same test in the future would lead to different results.

Negative, that's a good thing. And that's valuable to me as of now. But I'm still thinking well, is it going to be like this next year, months from now?

(P10, 62-year-old, female)

Despite the hesitation and potential misunderstanding exhibited by some of our participants, a few participants demonstrated knowledge of more complex genetics concepts when asked about the meaning of their results. These concepts included examples of penetrance and etiology, as highlighted below:

I think that just – I don't think that it's anything – anything is 100 percent. But I just think that maybe there's just some things that I may just not be predisposed to or that just are not genetic. It doesn't mean that you're not going to get them. It means it's not genetic.

(P9, 48-year-old, female)

3.5 | Understanding of residual risk

When asked if they were still at risk for the diseases included in the test panel after a negative genetic test result, all but one of the participants expressed that they had residual risk. However, the extent to which participants understood residual risk varied.

I think it lessens it [chances to develop cancer], but I think there are a lot of factors in life that can possibly change things.

(P1, 56-year-old, female)

Even participants who may have a less sophisticated understanding of genetics still seemed to understand that they should continue with routine screenings with their physician.

But it doesn't mean that something can't happen down the road and I would still kind of go through my normal medical treatments that my doctors would be [sic] would be having me watch for and things like that. So I think that I would go through those normal things and not have an attitude that I'm safe forever. I would definitely not have that attitude.

(P2, 49-year-old, female)

When asked about the sources of residual risk, most participants attributed remaining risk to environmental and behavioral factors.

What comes to mind immediately would be just lifestyle, maybe the type of work a person may have done, or maybe there's certain habits a person may have.

(P16, 63-year-old, male)

Many participants did not identify that other genetic factors could play a role in disease. However, when asked if they would have genetic testing again in the future, some were able to articulate that the testing they had in this study wasn't comprehensive.

3.6 | Personal value

There were five themes identified under personal value: peace of mind, self-knowledge, expectations not met, impact on lifestyle, and impact on healthcare choices. Participant conversations about the intended use and perceived value of their results often included expressions of gaining more control over their health through the knowledge they learned about themselves, which affirmed their lifestyle choices. Some participants with or at-risk for disease were disappointed to not learn about the cause of a disease in themselves or in their family.

3.7 | Peace of mind

A sentiment expressed by many participants was one of peace of mind after receiving their negative results. Some of these participants specifically expressed this relief in the context of their fears of developing a major health problem that could have been found through the testing. Others expressed a kind of relief in knowing they did not carry or pass on one of these genes to their children.

I guess it did impact my health because, like I said, my mind is at ease. [...] And I can't say they're not useful because they're very useful. They put my mind at ease.

(P17, 52-year-old, female)

About a third of the participants expressed during the interview that they were initially uncertain about pursuing genetic testing. However, everyone who expressed some level of indecision about pursuing testing also expressed peace of mind after receiving their negative test results.

3.8 | Self-knowledge

Another major aspect of personal value touched upon by participants was the value of gaining knowledge. Several individuals specifically stated that they were information seekers and the knowledge, in itself, provided value for them.

I think that it's better to have the knowledge than not to have it. So, I think it's just good to know one way or another. So, in that, knowledge is valuable in itself.

(P7, 35-year-old, female)

More generally, most participants expressed that genetic testing results contribute to information they seek about their overall health. Gaining this information satisfied not only curiosity but also provided them with self-knowledge:

It's more pieces of information, [...] having a health composite. [...] You know, it's sort of part of a whole health plan, so it just kind of gives me greater insight into how my body is working.

(P4, 64-year-old, male)

3.9 | Expectations not met

During the interviews, participants expressed that they had various expectations about the type of results they would receive when they first enrolled in the study. For

some participants, these expectations were not met, and those participants expressed disappointment. This disappointment related to both the type of information they hoped to receive from the test and the lack of risk information in the report, since participants received negative results.

Some participants were hoping to gain information about the etiology of personal disease. The majority of these participants expressed disappointment that no explanation was discovered through the testing.

It just leaves me still questioning what the causes are for the things that I do have.

(P7, 35-year-old, female)

Other participants expressed disappointment with the level of detail and risk information they received by mail. Participants were informed that their results were ‘Negative’ and were provided with a list of genes tested and an online link to their associated conditions. However, since participants expected to receive risk information, some felt the lack of this information limited utility of the results.

Again, my whole thing is that I was going in with the expectation of possibly receiving some analysis or breakdown of possible illnesses, or certain traits that I may develop over the years as I get older. And, since none of that was in the report.... So, since it didn’t provide me with any information, I didn’t find it useful.

(P8, 38-year-old, female)

3.10 | Impact on lifestyle

Participants also mentioned how they might use their results to make decisions about their health behaviors. All participants stated that these results would not cause them to change their current lifestyles.

There’s nothing like if I was genetically – if there was something genetic where I would modify some type of behavior, so there’s nothing for me to even think of modifying because it did not show anything.

(P9, 48-year-old, female)

However, many participants had misconceptions about genetic versus epigenetic modifications and the impact of lifestyle on a person’s DNA. These participants thought that lifestyle choices could have a direct impact on their genetic test results. They felt that the negative results reinforced their lifestyle choices and encouraged them to maintain their current health choices. When one participant was asked if the results caused her to change her health and lifestyle choices, she stated:

[Participant 14] ‘Because my choices are pretty clean and pretty holistic and pretty where you want people to be. It shows me I’m on the right track. [...] It shows me what I’m doing is what I should be doing’.

[Interviewer] ‘Do you believe that your lifestyle choices resulted in this negative result?’

[P14] ‘Yes’.

(56-year-old female)

3.11 | Impact on healthcare choices

Participants often brought up two ways genetic testing could impact their healthcare choices: sharing results with a healthcare provider and pursuing future genetic testing. Regardless of their opinion on the usefulness of the information, most participants expressed that they would share their results with their healthcare provider because they believed the practitioner should also find value in the results, even if no action was needed.

My internist – he should know my health, everything we know about it. He knows my family history, I've taken the time to collect all of that information. This is just another piece, another resource to have and to give us a more accurate picture of things.

(P3, 41-year-old, female)

When asked if participants would pursue future genetic testing, most stated that they would and gave a variety of reasons for testing. The comments illustrate the importance participants placed on understanding their own genetic information and using this knowledge to help them in the future. Some expressed an understanding that there are other genes not included in this test panel that could tell them more information about themselves. Others stated that if they were diagnosed with something that had a genetic cause, they would do additional testing for that specific condition. Most commonly, individuals expressed that they would do it so that they could enact preventative healthcare measures to offset predicted risk.

The same reason I did this [genetic testing study]. I think it's good to know. [...] Good to know what you might be predisposed to. Good to know what modifications you may make, in the future.

(P9, 48-year-old, female)

4 | DISCUSSION

Despite the highly educated nature of the study population, many participants expressed a lack of confidence in their knowledge of genetic concepts and were unsure of the relationship between genes, disease, and environment. These findings are consistent with Chapman et al. (2019), who showed that the overall genetic health literacy is low across all levels of education and professions (Chapman et al., 2019). However, others have argued that the general public does not need to understand the mechanics of genetic disease, but rather, what factors increase risk for genetic disease, like an extensive family history of breast cancer (Molster, Charles, Samanek, & O'Leary, 2009).

Findings from our study support the idea that having a poor understanding, or believing one has a poor understanding of genetic concepts did not interfere with participants' appreciation of their residual risk in relationship to their negative results. Participants in our study were able to correctly identify that environmental and behavioral factors could contribute to remaining risk, though few could identify that there were additional genetic factors that may also affect their risk. Residual risk was a key concept the authors wanted participants to

understand, as many in the genetics community have expressed concerns that consumers of DTC genetic testing may be less vigilant about lifestyle choices and recommended health screening as a result of their genetic testing (Brothers et al., 2019; Kaphingst et al., 2012; Ostergren et al., 2015). Consistent with DTC studies, nearly all participants in this study expressed that their negative results will not change their health behaviors or screening practices (Gordon et al., 2012; Kaphingst et al., 2012). Our study results are also consistent with Butterfield et al., which examined the impact of negative genomic screening results on healthy participants and found that the majority reported no plans to change their health behaviors (Butterfield et al., 2019).

However, several of our study participants had nuanced misconceptions about genetics that affected how they understood their negative genetic test results could impact future health decisions. These participants expressed that genes could change and that lifestyle choices have a direct impact on genetic test results. This idea of genomic instability seems to stem from confusion about the mechanism of disease, specifically the interaction between genes and lifestyle, and how lifestyle choices may cause disease. These findings are consistent with other studies showing that the public generally does not understand how genes cause or contribute to disease (Condit, 2010; Lucke, Hall, Ryan, & Owen, 2008). It has also been speculated that the general public's understanding of how genes relate to disease is often based on 'overly simplistic and a somewhat distorted understanding of basic genetic science and information' (Sabatello & Juengst, 2019). More concerning is that when asked about pursuing genetic testing in the future, some of our participants stated they would want to retake the test again to see how the results change over time. These findings have implications for the use of genetic testing in a healthy population (Molster et al., 2009). Additionally, these nuanced misconceptions highlight the important issue of what specifically individuals need to know about genetics in order to understand their genetic test results and make informed health decisions.

With regard to the personal value of the information gained from the genetic test results, most participants couched their views around the psychological impact of the results. Participants expressed gaining a 'peace of mind' from their results and the value of the information itself, which is consistent with studies of DTC genetic testing participants (Kohler, Turbitt, & Biesecker, 2017; Wasson, Sanders, Hogan, Cherny, & Helzlsouer, 2013). Some participants explained that their peace of mind was due to the belief that the test provided reassuring information about a concerning health problem, despite acknowledging there are other factors that contribute to disease risk. The somewhat contradictory finding that participants expressed understanding of residual risk while also feeling peace of mind in response to negative results bears further investigation. These findings could have major implications for genetic testing of relatively healthy populations, such as that being planned with the All of Us Research Program, if those who receive negative results are falsely reassured (Brothers et al., 2019; Collins & Varmus, 2015).

Another value of the results was the cognitive outcome of learning the information itself. Similar to other authors, many of our study participants expressed the idea that knowledge is power and preferred to have as much information as possible (Bollinger, Scott, Dvoskin, & Kaufman, 2012; Sanderson et al., 2016; Su, Howard, & Borry, 2011). Our participants

generally valued their results as an important piece of their overall health information. However, many participants expressed disappointment about the lack of detail and risk information they received from their results. Disappointment with the level of detail around the result not meeting expectations was also seen in a study conducted by Rego et al., where healthy participants who received exome sequencing results were underwhelmed by the type of information they received and had expectations of receiving more personalized risk information (Rego, Dagan-Rosenfeld, Bivona, Snyder, & Ormond, 2019). The high expectations for personalized risk information raise important considerations when extending genetic screening to the general population. Unrealistic expectations about the utility of genetic screening information could result in the overutilization by consumers and incorrect understanding about applications of negative genetic results.

4.1 | Limitations

While previous studies have investigated the impact of genetic testing in healthy populations (Butterfield et al., 2019; Kaufman, Bollinger, Dvoskin, & Scott, 2012; Ostergren et al., 2015; Sanderson et al., 2016; Zoltick et al., 2019), ours is among the first to explore understanding and personal value specifically for participants receiving negative, non-diagnostic genetic panel results. Participants in our study were highly educated, with all participants attending at least some college and the majority holding at least a college degree ($n = 14$, 82%). Previous studies on populations likely to pursue non-diagnostic testing are consistent with the demographics of participants in our study (Kaufman et al., 2012; Leighton, Valverde, & Bernhardt, 2012). However, our study population differed from most studies in that it was intentionally selected as a racially and ethnically diverse sample to better represent the heterogeneity of the general public: less than half of the participants identified as white ($n = 7$, 41%) and the rest identified as either black ($n = 5$, 29%) or Hispanic ($n = 5$, 29%). This diversity provides some additional perspective on how non-white US populations view negative results. Nevertheless, the highly educated nature of this study's population did not allow for the capture of a truly diverse sample. Past studies show that racial differences in genetic literacy may be correlated with education level (Haga et al., 2013; Ostergren et al., 2015). Moreover, the participants in this study had generally high household incomes, so a diversity of socioeconomic status was not captured. In addition, the participant population was too small to appreciate any difference in the described domains and themes based on demographic information.

This study is also limited by its exploratory nature in a small population. It is therefore, not generalizable to all individuals undergoing non-diagnostic genetic testing and receiving negative results. Participants in this study may be more favorable of and more motivated to pursue genetic testing than the general public since they participated in the eMERGE III study and this substudy. Additionally, no validated measures were used to assess participants' health or genetic literacy; investigators may have misconstrued participants' difficulty explaining genetic concepts as confusion.

4.2 | Practice implications

This study has important implications for genetic counselors who will be increasingly involved in the design of studies and programs that offer genetic testing and return of results

to healthy populations and raises many questions about the considerations of extending genetic testing to a wider audience. This research suggests what others have found in both research and DTC settings; that healthy populations or populations having non-diagnostic genetic testing may have different educational requirements than those obtaining diagnostic testing. Our results suggest that basic education focused on genetic heterogeneity, and the contributions of genes, lifestyle, and environmental factors to disease and disease risk, may be as important as information about residual risk. It is also critical that healthy populations undergoing genetic testing have a clear idea of the limitations of testing and may require additional information relating to future testing.

4.3 | Future research

These results need to be confirmed with studies in larger and more diverse populations. Concerning personal utility, two areas should be explored with population screening in mind: perceived personal risk in healthy populations and participant expectations of explanations for diseases of unknown or non-genetic etiology. Finally, it is essential that larger, more socioeconomically diverse cohorts with varied levels of education are studied to more fully explore the impact of population screening.

5 | CONCLUSION

This research provides insight into participant understanding and personal utility of negative, non-diagnostic genetic test results in a racially and ethnically diverse population. Findings echo what has been seen with users of DTC genetic testing; that participants expressed a limited understanding of genetics and sources of individual risk. However, this limited understanding did not appear to affect their understanding about residual risks. Additionally, there were some misunderstandings about disease etiology that could potentially impact healthcare choices in the future, such as the belief that genes can change and are impacted by lifestyle choices. Participants also expressed that their negative results had personal utility even if they had limited clinical utility, though several participants had unmet expectations that the testing could provide more individualized results. Findings in this study can aid efforts to improve or innovate scalable modes of result return that foster comprehension following negative genetic testing and address expectations before testing.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data Sharing and Data accessibility

The data obtained for this study are not available publicly.

REFERENCES

- ACMG Board of Directors (2015). ACMG policy statement: updated recommendations regarding analysis and reporting of secondary findings in clinical genome-scale sequencing. *Genetics in Medicine*, 17(1), 68–69. 10.1038/gim.2014.151. [PubMed: 25356965]
- Bollinger JM, Scott J, Dvoskin R, & Kaufman D (2012). Public preferences regarding the return of individual genetic research results: findings from a qualitative focus group study. *Genetics in Medicine*, 14(4), 451–457. 10.1038/gim.2011.66. [PubMed: 22402755]
- Brothers KB, Vassy JL, & Green RC (2019). Reconciling opportunistic and population screening in clinical genomics. *Mayo Clinic Proceedings*, 94(1), 103–109. 10.1016/j.mayocp.2018.08.028. [PubMed: 30611438]
- Burke W, Coughlin SS, Lee NC, Weed DL, & Khoury MJ (2001). Application of population screening principles to genetic screening for adult-onset conditions. *Genetic Testing*, 5(3), 201–211. 10.1089/10906570152742245 [PubMed: 11788085]
- Butterfield RM, Evans JP, Rini C, Kuczynski KJ, Waltz M, Cadigan RJ ... Henderson GE (2019). Returning negative results to individuals in a genomic screening program: lessons learned. *Genetics in Medicine*, 21(2), 409–416. 10.1038/s41436-018-0061-1. [PubMed: 29875426]
- Chapman R, Likhanov M, Selita F, Zakharov I, Smith-Woolley E, & Kovas Y (2019). New literacy challenge for the twenty-first century: genetic knowledge is poor even among well educated. *Journal of Community Genetics*, 10(1), 73–84. [PubMed: 29589204]
- Collins FS, & Varmus H (2015). A new initiative on precision medicine. *New England Journal of Medicine*, 372(9), 793–795. 10.1056/NEJMp1500523.
- Condit CM (2010). Public understandings of genetics and health. *Clinical Genetics*, 77(1), 1–9. 10.1111/j.1399-0004.2009.01316.x. [PubMed: 20092586]
- Corbin J, & Strauss A (1990). Grounded theory research - Procedures, canons and evaluative criteria. *Zeitschrift Fur Soziologie*, 19(6), 418–427. 10.1007/Bf00988593.
- Dorschner MO, Amendola LM, Turner EH, Robertson PD, Shirts BH, Gallego CJ ... Jarvik GP (2013). Actionable, pathogenic incidental findings in 1,000 participants' exomes. *The American Journal of Human Genetics*, 93(4), 631–640. 10.1016/j.ajhg.2013.08.006. [PubMed: 24055113]
- eMERGE C (2019). Harmonizing clinical sequencing and interpretation for the eMERGE III network. *The American Journal of Human Genetics*, 105(3), 588–605. 10.1016/j.ajhg.2019.07.018. [PubMed: 31447099]
- Gordon ES, Griffin G, Wawak L, Pang H, Gollust SE, & Bernhardt BA (2012). "It's not like judgment day": public understanding of and reactions to personalized genomic risk information. *Journal of Genetic Counseling*, 21(3), 423–432. 10.1007/s10897-011-9476-4. [PubMed: 22180182]
- Green RC, Berg JS, Grody WW, Kalia SS, Korf BR, Martin CL ... Genomics. (2013). ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. *Genetics in Medicine*, 15(7), 565–574. 10.1038/gim.2013.73. [PubMed: 23788249]
- Haga SB, Barry WT, Mills R, Ginsburg GS, Svetkey L, Sullivan J, & Willard HF (2013). Public knowledge of and attitudes toward genetics and genetic testing. *Genetic Testing and Molecular Biomarkers*, 17(4), 327–335. 10.1089/gtmb.2012.0350. [PubMed: 23406207]
- Haga SB, Mills R, Pollak KI, Rehder C, Buchanan AH, Lipkus IM ... Datto M (2014). Developing patient-friendly genetic and genomic test reports: formats to promote patient engagement and understanding. *Genome Medicine*, 6(7), 58. 10.1186/S13073-014-0058-6. [PubMed: 25473429]
- Hershberger RE, Givertz MM, Ho CY, Judge DP, Kantor PF, McBride KL ... Ware SM (2018). Genetic evaluation of cardiomyopathy-a heart failure society of America practice guideline. *Journal of Cardiac Failure*, 24(5), 281–302. 10.1016/j.xcardfail.2018.03.004. [PubMed: 29567486]
- Kaphingst KA, McBride CM, Wade C, Alford SH, Reid R, Larson E ... Brody LC (2012). Patients' understanding of and responses to multiplex genetic susceptibility test results. *Genetics in Medicine*, 14(7), 681–687. 10.1038/gim.2012.22. [PubMed: 22481132]

- Kaufman DJ, Bollinger JM, Dvoskin RL, & Scott JA (2012). Risky business: risk perception and the use of medical services among customers of DTC personal genetic testing. *Journal of Genetic Counseling*, 21(3), 413–422. 10.1007/s10897-012-9483-0. [PubMed: 22278220]
- Kohler JN, Turbitt E, & Biesecker BB (2017). Personal utility in genomic testing: a systematic literature review. *European Journal of Human Genetics*, 25(6), 662–668. 10.1038/ejhg.2017.10. [PubMed: 28295040]
- Leighton JW, Valverde K, & Bernhardt BA (2012). The general public's understanding and perception of direct-to-consumer genetic test results. *Public Health Genomics*, 15(1), 11–21. 10.1159/000327159. [PubMed: 21720148]
- Lucke J, Hall W, Ryan B, & Owen N (2008). The implications of genetic susceptibility for the prevention of colorectal cancer: A qualitative study of older adults' understanding. *Community Genetics*, 11(5), 283–288. 10.1159/000121399. [PubMed: 18493126]
- MacQueen KM, McLellan E, Kay K, & Milstein B (1998). Codebook development for team-based qualitative analysis. *Cultural Anthropology Methods*, 10(12), 31–36.
- Molster C, Charles T, Samanek A, & O'Leary P (2009). Australian study on public knowledge of human genetics and health. *Public Health Genomics*, 12(2), 84–91. 10.1159/000164684. [PubMed: 19039252]
- Nightingale BM, Hovick SR, Brock P, Callahan E, Jordan E, Roggenbuck J, ... Morales A (2019). Hypertrophic cardiomyopathy genetic test reports: A qualitative study of patient understanding of uninformative genetic test results. *Journal of Genetic Counseling*, 28(6), 1087–1097. 10.1002/jgc4.1159. [PubMed: 31408576]
- Ostergren Jenny E., Gornick Michele C., Carere Deanna Alexis, Kalia Sarah S., Uhlmann Wendy R., Ruffin Mack T., Group, P. G. S (2015). How well do customers of direct-to-consumer personal genomic testing services comprehend genetic test results? Findings from the impact of personal genomics study. *Public Health Genomics*, 18(4), 216–224. 10.1159/000431250. [PubMed: 26087778]
- Recchia G, Chiappi A, Chandratillake G, Raymond L, & Freeman ALJ (2020). Creating genetic reports that are understood by nonspecialists: a case study. *Genetics in Medicine*, 22(2), 353–361. 10.1038/s41436-019-0649-0. [PubMed: 31506646]
- Rego S, Dagan-Rosenfeld O, Bivona SA, Snyder MP, & Ormond KE (2019). Much ado about nothing: A qualitative study of the experiences of an average-risk population receiving results of exome sequencing. *Journal of Genetic Counseling*, 28(2), 428–437. 10.1002/jgc4.1096 [PubMed: 30835913]
- Sabatello M, & Juengst E (2019). Genomic essentialism: Its provenance and trajectory as an anticipatory ethical concern. *Hastings Center Report*, 49, S10–S18.
- Sanderson SC, Linderman MD, Suckiel SA, Diaz GA, Zinberg RE, Ferryman K, Schadt EE (2016). Motivations, concerns and preferences of personal genome sequencing research participants: Baseline findings from the HealthSeq project. *European Journal of Human Genetics*, 24(1), 153. 10.1038/ejhg.2015.179. [PubMed: 26508568]
- Saunders B, Sim J, Kingstone T, Baker S, Waterfield J, Bartlam B, ... Jinks C (2018). Saturation in qualitative research: exploring its conceptualization and operationalization. *Quality & Quantity*, 52(4), 1893–1907. 10.1007/s11335-017-0574-8. [PubMed: 29937585]
- Singer N(2018). Employees Jump at Genetic Testing. Is That a Good Thing?. NY Time. Retrieved from <https://www.nytimes.com/2018/04/15/technology/genetic-testing-employee-benefit.html>
- Su Y, Howard HC, & Borry P (2011). Users' motivations to purchase direct-to-consumer genome-wide testing: an exploratory study of personal stories. *Journal of Community Genetics*, 2(3), 135–146. 10.1007/s12687-011-0048-y [PubMed: 22109820]
- Tandy-Connor S, Guiltinan J, Krempely K, LaDuca H, Reineke P, Gutierrez STippin Davis B (2018). False-positive results released by direct-to-consumer genetic tests highlight the importance of clinical confirmation testing for appropriate patient care. *Genetics in Medicine*, 20(12), 1515–1521. 10.1038/gim.2018.38 [PubMed: 29565420]
- Wasson K, Sanders TN, Hogan NS, Cherny S, & Helzlsouer KJ (2013). Primary care patients' views and decisions about, experience of and reactions to direct-to-consumer genetic testing: a

longitudinal study. *Journal of Community Genetics*, 4(4), 495–505. 10.1007/s12687-013-0156-y [PubMed: 23832288]

Yang Y, Muzny DM, Xia F, Niu Z, Person R, Ding Y, ... Eng CM (2014). Molecular findings among patients referred for clinical whole-exome sequencing. *JAMA*, 312(18), 1870–1879. 10.1001/jama.2014.14601. [PubMed: 25326635]

Yurgelun MB, Hiller E, & Garber JE (2015). Population-wide screening for germline BRCA1 and BRCA2 mutations: Too much of a good thing? *Journal of Clinical Oncology*, 33(28), 3092–3095. 10.1200/JCO.2015.60.8596. [PubMed: 26282646]

Zoltick Emilie S., Linderman Michael D., McGinniss Molly A., Ramos Erica, Ball Madeleine P., Church George M. ... PeopleSeq C (2019). Predispositional genome sequencing in healthy adults: design, participant characteristics, and early outcomes of the PeopleSeq Consortium. *Genome Medicine*, 11(1), 10. 10.1186/S13073-019-0619-9. [PubMed: 30808425]

TABLE 1

Demographics of the study participants (self-reported)

Sex	Male	3 (18%)
	Female	14 (82%)
Race/Ethnicity	White	7 (41%)
	Black	5 (29%)
	Hispanic	5 (29%)
Age	Mean	53
	Median	56
	Range	35-65
Profession	Healthcare provider	4 (24%)
	Other	13 (76%)
Education	Some college (or certificate)	3 (18%)
	College graduate	7 (41%)
	Postgraduate degree (e.g., MA, MS, PhD, MD, DO)	7 (41%)
Income	\$15,000-\$29,999	1 (6%)
	\$30,000-\$44,999	3 (18%)
	\$45,000-\$59,999	3 (18%)
	\$60,000-\$89,999	4 (24%)
	\$90,000-\$149,999	2 (12%)
	\$150,000-\$199,999	2 (12%)
	\$200,000 or above	2 (12%)
Religiosity	Very religious	4 (24%)
	Somewhat religious	11 (64%)
	Not religious	2 (12%)
Previous genetic testing	Yes	3 (18%)
	No	14 (82%)

TABLE 2

Themes identified through data analysis

Domain	Theme	Category
Comprehension	1. Participants expressed both a lack of understanding and a lack of confidence in their understanding of genetics concepts.	• Most participants expressed that they do not understand genetics concepts. • Some participants expressed confusion about genetics concepts. • Some participants expressed a lack of confidence in their understanding of genetic concepts while going on to describe these same concepts accurately. • Few participants expressed knowledge of more complex genetic concepts.
	2. Participants demonstrated a knowledge of some genetic concepts, particularly when it came to residual risk. They understood that there is residual risk for diseases included in this testing and the testing is not comprehensive.	• Participants understood that lifestyle choices and environmental factors could contribute to diseases included in this testing.
Personal Value		• Most participants understood they should continue with routine screening with their physician. • Most participants did not identify genetic factors as a source of residual risk
	1. Participants expressed that these results held personal value as they provided peace of mind.	• Many participants expressed peace of mind as a reaction to the apprehension of receiving a positive result.
	2. Participants expressed that these results held personal utility and value as they provided knowledge of self.	• All participants expressing uncertainty about undergoing testing were ultimately relieved with their results. • Participants wanted the information about themselves as they found value in this knowledge.
	3. Participants with specific expectations about their results and the report they would receive were disappointed when these expectations were not met.	• Most participants expressed that genetic testing is a part of participants' overall health information. • Participants expecting an explanation for personal history of disease oftentimes expressed disappointment that the results were negative.
	4. Participants expressed that these results encourage them to maintain their lifestyles.	• Some participants were disappointed about not receiving a report containing detailed risk information. • Most participants expressed that these results would result in no change to their lifestyles.
	5. Participants expressed ways that genetic testing impacted their healthcare choices.	• Some participants expressed that these results reinforced their lifestyle choices. • Most participants expressed that they would share their genetic test results with their healthcare providers.
		• Most participants would go through genetic testing in the future.